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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/939,119	08/24/2001	Robert J. Lipshutz	AFFYP016C1	3568

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EXAMINER	
RILEY, JEZIA	

ART UNIT	PAPER NUMBER
1637	4

DATE MAILED: 04/05/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/939,119	LIPSHUTZ ET AL.	
	Examiner	Art Unit	
	Jezia Riley	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-7 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The art unit for this application has changed. Applicant is informed, that any future response should be directed to Art Unit 1637.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to an array of probes that are complementary to the target nucleic acid sequence. There is no disclosure of negative controls that are to be used to select complementary segments for specific probes.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In Re Colianni,* 195 USPQ 150 (CCPA 1977) and have been adopted by the Board Appeals and Interferences in *Ex Parte Forman,* USPQ 546 (BPAI 1986).
Among these factors are: the nature of the invention, the state of the prior art, the predictability or lack thereof in the art, the breadth of the claims, the amount of direction or guidance present, and the presence or absence of working examples.

Breadth of the claims:

The claims are broadly drawn to an array of oligonucleotide probes that are complementary to a target. In the embodiments of claims there is no disclosure of

negative controls that are to be used to select complementary segments for specific probes especially of small size that are useful as probes.

Amount of direction/guidance

A broad possible range for negative controls are possible and in order to enable the selection of useful probes there is a need to set forth which negative controls is (are) to be used. Is there one organism that would be the negative control or a panel of organisms that would be the negative controls? It is undue experimentation to collect nucleic acids probes, among the unspecified great number of organism, and to sequence them to determine the ones that would be used to detect the target in order to practice the broad scope of claims. This is clearly an invitation to experiment to select such a probe to make it specific to said polymorphic nucleic acid . These leave the entire work of finding probes up to someone wishing to practice claims 1-7 which is undue experimentation. Stackebrandt et al. (Patent # 5,089,386) disclose nucleic acid fragment capable of hybridizing to rRNA of *Listeria monocytogenes* and not to rRNA of *Bacillus subtilis.* They show a probe development strategy comprising: (1)Identifying regions of rRNA which might be useful as a target sites for nucleic acid hybridization probes. (2) These nucleotides sequences were compared to one another and to other rRNA nucleotide sequences. (3) Testing each nucleic acid probe is required. (4) Then first generation probes are designed and several other consideration are taken in count such as the geometry of the probe itself and self complementarity for example. In aggregate, the set of probes will detect most or al Listeria and few or no non-listeria. Then the final step of probe design is to test the probes on real samples. (col.4 to col. 7). In col. 3, lines 6-19 the authors state that probes to Listeria rRNA target sequences which are sufficiently similar in a significant number of Listeria that one or a few probes

can hybridize to the target region in those Listeria and are sufficiently different in most non-Listeria rRNAs, that under some conditions where the probe(s) hybridize to Listeria rRNAs, they are not capable of hybridizing, or very poorly, to most non-Listeria rRNAs.

Therefore given the unpredictability of the art and the lack of guidance in the specification, it is the Examiner's position that one skilled in the art (the Ph.D. degree with laboratory experience) could not perform the method of the claims as broadly recited without undue experimentation. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-7 are rejected under 35 U.S.C. § 102(a) as being anticipated by Lipshutz et al. (Biotechniques, Vol. 19, No. 3, pp. 442-447).

Lipshutz et al. described the use of oligonucleotide probe arrays to access genetic diversity. The target nucleic acid is labeled with a fluorescent reporter group and incubated with the array. If the target nucleic acid has regions complementary to probes on the array, then the target will hybridize with those probes. The fraction of probes bound to targets will vary with the base composition of the probe and the extent of target-probe match. Probes matching the target will hybridize more strongly than with

mismatches, insertions and deletions (pp.443-444, bridging paragraph). The oligonucleotide arrays can be designed and used to rapidly and efficiently screen characterized genes for polymorphism (p. 445, col. 1 and p. 446, col. 3). Dedicated instrumentation and software have been developed for array hybridization, fluorescent detection and data acquisition and analysis (p. 446, col. 3).

The 35 U.S.C. § 102(a) rejection is based on the difference in the instant inventor list and the autorship list of the reference. Katz type declaration may possibly overcome the rejection.

5. Claims 1-7 are rejected under 35 U.S.C. § 102(b) as being anticipated by Southern et al. (Genomics, Vol. 13, pp. 1008-1017, 1992).

Southern et al. teach a method for making complete sets of oligonucleotides of defined length. They were used to explore factors affecting molecular hybridization. Specific motifs can be incorporated into all sequences of the array to focus analysis on sequences of biological interest. They also show how image processing procedures can be applied to the results for rapid analysis of mutation. In page 1014, they apply 2 set of probes (sequences I and II) that differ only by one C to T substitution. The strong difference between the two hybridization patterns suggest a more direct way of finding the underlying sequence difference. As the two images were produced from the same plates, they can be overlaid, and one image can be subtracted from the other (Figure 4). This reduces the intensity of the spots that are in common, emphasizing those that differ in the two images.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 703-305-6855. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

April 3, 2002

JEZIA RILEY
PRIMARY EXAMINER